Evaluating isolation and contact tracing to control pandemic potential influenza outbreaks

Joshua W. Lambert

Abstract

Introduction

Infectious disease outbreaks pose an everpresent public health threat. The COVID-19 pandemic caused over 7 million deaths (WHO COVID-19 Dashboard), while the 1918 influenza pandemic caused an estimated $\sim$50 million deaths (Johnson and Mueller, 2002). Less transmissible pathogens, such as Ebola, can cause sustained outbreaks leading to the excess death of thousands (WHO Ebola Response Team, 2014). Thus, timely and accurate response is critical early in an outbreak when the pandemic or epidemic potential is still uncertain (Kucharski, 2024). An effective response requires understanding the efficacy and feasibility of intervention strategies across pathogens with varying epidemiological characteristics (Fraser et al., 2004).

The likelihood of an outbreak being controlled, in other words going locally-extinct or -eliminated, is in part based on the epidemiological characteristics of the pathogen, and in part on the inventions implemented, both pharmaceutical and non-pharmaceutical. The primary epidemiological determinant for the spread of an infectious disease is the reproduction number (R), defined as the average number of secondary cases per primary case. The higher the reproduction number the less likely a disease, without intervention, is to cease transmission in a population. If a pathogen is subcritical (i.e. $R < 1$) it will eventually stop spreading but can still cause transient outbreaks (Farrington and Grant, 1999). Individual-level heterogeneity in transmission also influences the possibility of a pathogen going extinct from stochasticity in the transmission process (Lloyd-Smith et al., 2005). Higher individual-level variation for a given reproduction number leads to, on average, more outbreaks being controlled (however a small number of outbreaks may become large due to superspreading). In addition, the likelihood of containment is reduced — assuming $R > 1$ — if there are multiple introductions into a populations (Kucharski et al., 2020).

A range of interventions can be deployed to reduce or prevent the transmission of infectious diseases, broadly classified into pharmaceutical and non-pharmaceutical interventions (NPIs). Early in an outbreak — especially in the case of a novel pathogen — NPIs are often the first line of defence, as pharmaceutical options may not yet be available. These interventions vary in scope and specificity, from targeted measures such as isolation and contact tracing, to broader actions like school closures, bans on gatherings, and regional or national lockdowns (Huag et al., 2020). The success of such interventions in containing an outbreak before it becomes sustained and widespread depends on several factors, including the type of intervention, the delay before implementation, and the intervention's effectiveness (Longini et al., 2005). For highly transmissible pathogens (e.g. $R \geq 2.5$) with short generation times (e.g. ≤ 3 days), swift and effective interventions are required to achieve containment. Pathogens that have a large proportion of onward transmission prior to symptom onset (latent period shorter than incubation period) or have asymptomatic (subclinical) cases are less easily controlled (Fraser et al., 2004).

Isolation of infected individuals aims to break the chain of transmission by preventing further infection of susceptible individuals. The earlier an infectious case can be isolated, the more effective it is at averting secondary cases, with isolation prior to infectiousness optimal. This is challenging for most pathogens because infectiousness preceeds prodromal symptoms. While contact tracing is the process of finding the contacts of infected individuals. Both isolation and contact tracing are often used NPIs to try and curtail the growth of an epidemic. Contact tracing can be forward, whereby infected individuals are asked who they have been in contact with so their contacts can be followed-up and isolated or quarantined if needed; or backward contact tracing whereby infected individuals are asked who they have been in contact with prior to being infected to identify the source of infection and potentially forward trace from the source. Isolation and contact tracing is a targeted approach, like ring vaccination, that looks to prevent the onward transmission of an infectious disease by tackling infected individuals and their contacts (Kucharski et al., 2016; Ferretti et al., 2020; Keeling et al., 2020; Whittaker et al., 2024). Isolation or vaccination of traced individuals has proved widely effective in controlling different outbreaks with a variety of pathogens differing in their aetiological and epidemiological characteristics (Foege et al., 1971; Bell and World Health Organization Working Group on International and Community Transmission of SARS, 2004). However, it's important to remember that it's not a panacea for all outbreak scenarios. In epidemics or pandemics where the proportion

of cases or contacts missed is high, either because surveillance is patchy or because the number of contacts exceeds the capacity of the system, the efficacy of contact tracing to contain an outbreak diminishes, or at worst, fails completely (Dhillon and Srikrishna, 2018; Hellewell et al., 2020).

It has become widely accepted that influenza viruses cannot be controlled with isolation and contact tracing because the rate at which infected individuals become infectious and transmit is faster than the latency in the process of isolating contacts (Fraser et al., 2004; Klinkenberg et al., 2006). However, with the recent human infections of avian influenza (A/H5N1), mostly among poultry and cattle farmers (Garg et al., 2025) and the longer estimates of incubation period and serial interval from historical H5N1 data (Ward et al., 2024) it may be that isolation and contact tracing is able to control influenza. The (antigenic) novelty of a pathogen introduced into a human population is a leading risk factor for causing a pandemic. Thus, influenza subtypes that have negligible levels of existing immunity in the population are probable epidemic and pandemic candidates. This is the case for H5N1 (Ward et al., 2024) and H7N9 (Tanner et al., 2015) and was the case when H1N1 caused an outbreak in 2009 (Fraser et al., 2009). Historically, avian influenza (H5N1 and H7N9) has had high severity (case fatality risk $\sim 35\% - 55\%$), and therefore sustained transmission in a human population could have substantial mortality and morbidity implications (Tanner et al., 2015).

In this study we evaluate the effectiveness of controlling infectious disease outbreaks that exhibit influenza-like epidemiological characteristics using a mathematical model. In effect the ability to control an epidemic with isolation and contact tracing is a race between the identification and isolation of contacts and the spread of the infectious agent (Reyna-Lara et al., 2021). The dogma that influenza contagion outpaces our ability to trace and isolate in time, may not hold for all pathogen subtypes with new estimates of incubation period and serial interval (Ward et al., 2024). This study looks to define the speed and effectiveness of isolation under different response delays across epidemic scenarios to inform outbreak response; quantifying the impact of reducing the delay to isolation on outbreak containment and the utility of rapid testing.

Methods

Branching process model with isolation

To assess the efficacy of isolation and contact tracing to control an outbreak of pandemic-potential influenza we used an individual-level transmision model implemented in the R package `{ringbp}` (Hellewell et al., 2025) (Figure 1). The epidemic simulation model uses a single-type branching process with a negative binomial offspring distribution to simulate the spread of a pathogen through a population (infinite population size, without depletion of susceptibility). The mean of the negative binomial offspring distribution is the basic reproduction number (R), and this distribution allows the model to be parameterised to capture overdispersion of transmission, in other words, some infectors are superspreaders and infect a disproportionate number of individuals (Lloyd-Smith et al., 2005; Kucharski et al., 2020).

There are three categories for individuals in the simulation, with each having their own parameterisation for the negative binomial offspring distribution: 1) *community* (i.e. general population), 2) *isolated*, and 3) *asymptomatic*. Each group have a distinct R and dispersion (k) parameter due to the assumed differences in transmission dynamics between groups.

The time between an infector being infected and then infecting an infectee (i.e. generation time) is indirectly computed using the incubation period (which samples the symptom onset time from the exposure time of each case) and sampling from a skew-normal distribution (Azzalini, 1985). This controls the proportion of the infections that occur prior to, or after, the symptom onset of an infector. The symptom onset time is used as the location parameter (ξ) of the distribution, providing the point around which the distribution is dispersed. The scale parameter (ω) is fixed at two, this parameter (with the shape parameter) defines the variance of the distribution. We select this value as to provides a realistic amount of variance when transforming onset time to exposure time (variance range for scenarios in this study: 1.5 - 3.2). The shape parameter (α) defines the skewness of the distribution, whereby positive values cause right-skewed values distribution around the location ξ, and negative values have the opposite effect (as $\alpha \to \infty$, the skew-normal converges to a folded-normal distribution). In summary, for a given parameterisation of the skew-normal distribution given the time of symptom onset (ξ) and fixing ω and α we sample the time an infectee is exposed/infected by an infector.

The NPI implemented in the transmission model is an isolation of symptomatic cases and contact tracing (Figure 1). When a case is symptomatic they are isolated after a delay. The timing of isolation is drawn from the onset-to-isolation distribution (see Pathogen epidemiological parameters section for parameterisation). Any infection times that are sampled to occur after the isolated of an infector are remove, because isolation is assumed completely effective at preventing further transmission, reducing the number of secondary cases if the speed of isolation is quicker than some or all of the secondary infection times. In other words, once a case is isolated at time $t_{isolated}$, the probability of that case infecting anyone at $t > t_{isolated}$ is zero. Another way to interpret the model is that R is composed of secondary infections before isolation (R_{pre}) and secondary infections after an assumed isolation time ($R_{isolated}$). Symptomatic individuals that are traced are

isolated either when 1) the onset-to-isolation delay after symptom onset, or 2) the infector is isolated. The isolation of the infectee is whatever occurs first of these two events.

There are several mechanisms where isolation and contact tracing are imperfect at reducing onward disease transmission. The proportion of contacts missed by contact tracing is defined by the proportion of ascertainment and can range between zero, that is nobody is traced, to one, every case is traced. Symptomatic cases that have been missed when contact tracing their infectors are isolated at the onset-to-isolation delay after their symptom onset time. Additionally, contact tracing misses infections by an asymptomatic infector. In this event the infectees are missed by contact tracing owing to the infector not being known to the response system.

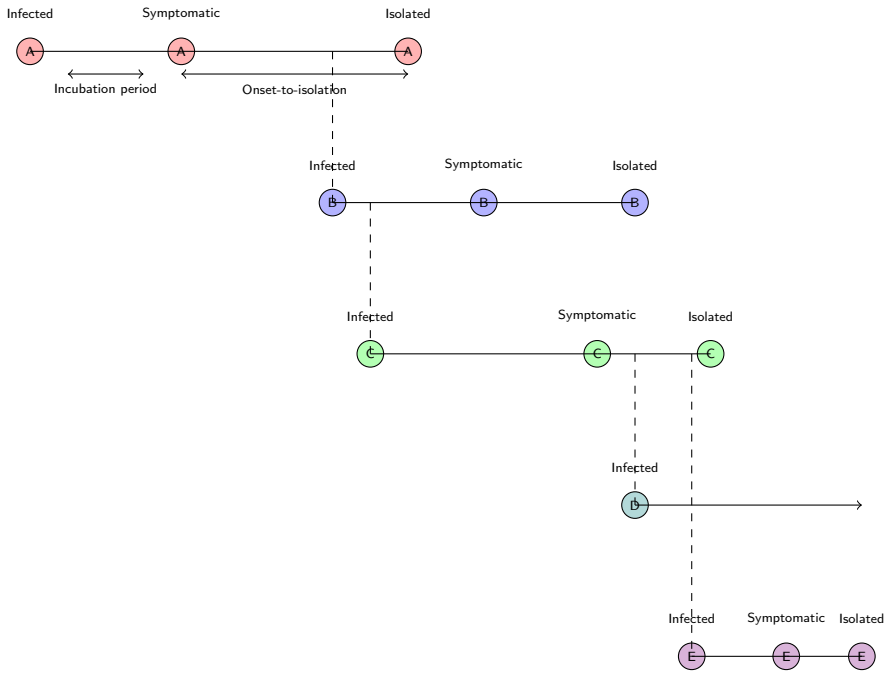

Figure 1: A schematic of the branching process model with isolation.

Defining outbreak control

We use the same definition for outbreak control as Hellewell et al. (2020): no new cases between 12 and 16 weeks after the start of an outbreak. The rationale for this criteria is that some outbreaks that do not take off and become large may still have a few cases for the first few weeks of an outbreak, therefore the window for control needs to be enough time after the seeding of an outbreak to be sure it is extinct.

There is also a maximum number of cases in simulation model, that when reached is judged to have reached a large epidemic and not controllable with 12-16 weeks. We set this limit to 500 cases. This number needs to be larger than the expected cluster size from an subcritical outbreak produce by chance (i.e. larger than $N_i/(1-R)$, where N_i is the number of initial cases and R is the reproduction number).

Pathogen epidemiological parameters

In this study we evaluate the feasibility of controlling outbreaks of selected influenza subtypes that have previous caused sporadic human-to-human outbreaks with pandemic potential. We include A/H5N1, A/H1N1, and A/H7N9. These have caused outbreaks of various size and severity over the past 100 years. H5N1 has caused small outbreaks ($<$ 10 cases) of human-to-human transmission (Yang et al., 2007; Aditama et al., 2012). H1N1 is now an endemic seasonal influenza with substantial population immunity, but a novel strain, H1N1pdm09, emerged in 2009 and caused a pandemic outbreak (Fraser et al., 2009; Lessler et al., 2009).

We extracted incubation periods from the epidemiological literature that have been previously estimated for the chosen Influenza subtypes. All incubation periods were found to be well described by a Weibull distribution, Nishiura and Inaba (2011) report the best fitting Weibull shape and scale parameters for H1N1 to be 1.77 and 1.86, respectively (Figure 3). Cowling et al. (2013) report the incubation period for H5N1 and H7N9, both Weibull distributed. For H5N1 the Weibull

distribution has a mean of 3.3 days and standard deviation (SD) of 1.5 days, for H7N9 the Weibull distribution has a mean of 3.1 days and SD 1.4 days (Cowling et al., 2013) (Figure 3).

The reproduction number (R) use to simulate transmission for each influenza subtype was 1.1, 1.5, 2.5 and 3.5. We chose these values and they represent either similar values to previously estimated R values for influenza outbreaks (Ferguson et al., 2006), including H1N1 (Fraser et al., 2009; Lessler et al., 2009), or they represent an inflated values of current estimates of H5N1 and H7N9 subtypes to evaluate the effectiveness of isolation and contact tracing in the event that pathogen evolution (e.g. genetic reassortment (Peacock et al., 2025) or mutations in receptor binding preference (Lin et al., 2024)) enhances the human-to-human transmissibility of these pathogens. Current estimates for H5N1 and H7N9 subtypes are below unity (i.e. $R < 1$) (Tanner et al. 2015; Ward et al. 2024, but see Yang et al. 2007 for a H5N1 R estimate above 1) so transmission is expected to stop without intervention; with most outbreaks being small except in rare instances of superspreading events. Therefore evaluating isolation and contact tracing requires simulating outbreaks that have pandemic potential with exponential spread in the absence of control measures.

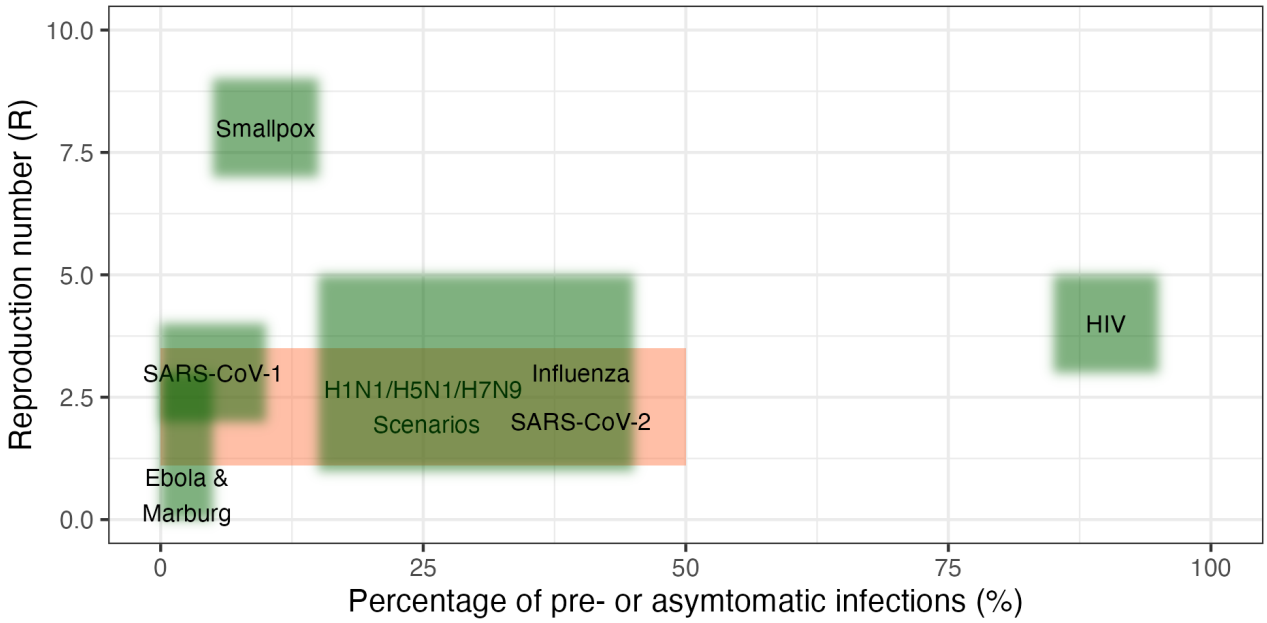

Figure 2: The pathogen characteristics, in terms of tranmissibility (R) and proportion of disease transmission that occurs before the onset of symptoms (including cases that are entirely asymptomatic). The figure includes: Influenza, SARS-CoV-1, SARS-CoV-2, Smallpox, Ebola, Marburg, and HIV shown by green shaded areas. The size of the shaded area reflects the differences in pathogen characteristics, both between variants and outbreaks, the blurred edges reflects uncertainty in parameter estimates. The parameter space of transmissibility and pre- and asymptomatic transmission explored in this paper is shown in the orange box.

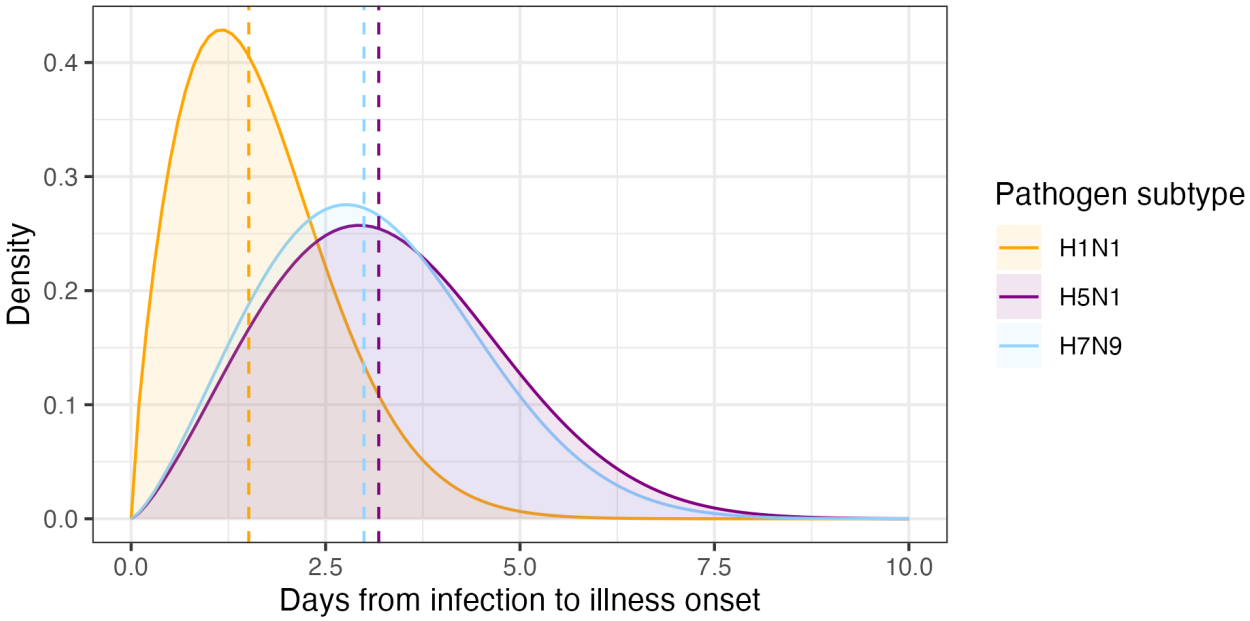

Figure 3: Incubation period for the Influenza subtypes: H1N1, H5N1 and H7N9.

Simulation scenarios

To assess under what scenarios pandemic-potential influenza outbreaks could be contained with the use of isolation and contact tracing we set up a simulation experiment. We defined a parameter space to explore across a variety of epidemiological characteristics (as defined in Pathogen epidemiological parameters section), contact tracing effectiveness, proportion of aysmptomatic cases and presymptomatic transmissin, and number of initial cases.

The ability to contain an outbreak by isolating infected individuals is highly contingent on the response time, or delay, between individuals becoming symptomatic, getting tested, the test results being returned and going into isolation. The probability that this series of steps will take an given amount of time is encapsulated in the onset-to-isolation delay distribution, i.e. onset-to-isolation distribution determines the time between a case developing symptoms and then becoming isolated. Here we define the onset-to-isolation as a response time as it is determined by the time delay between an individual responding to symptoms by getting tested and the turn around time for the tests to be analysed and the result returned. We view the onset-to-isolation as a feature of the public health outbreak response rather than an epidemiological characteristic of a disease. As such it is possible for pandemic response to adapt their response time to meet the needs of an outbreak.

We assume that an isolated case cannot transmit, so isolation is assumed to be 100% effective once enacted ($R_{isolated} = 0$). The onset-to-isolation delay is parameterised with three scenarios: a fast response, based on the SARS in Hong Kong (Donnelly et al. 2003) and a slower response based on COVID-19 in Wuhan, China (Li et al. 2020) (Figure 4). Both the fast and slow onset-to-isolation are parameterised as Weibull distributions, the SARS-like distribution has shape (λ) 1.65 and scale (k) 4.29 (mean = 3.83 days, SD = 2.38 days), the COVID-like distribution has shape = 2.31 and scale = 9.48 (mean = 8.40, SD = 3.87 days) (Figure 4). These two empirically informed delay distributions provide a guide to possible response times in the case of an influenza outbreak and will enable us to evaluate if such delays are too long to contain a disease that can transmit rapidly such as influenza. We also include a third onset-to-isolation scenario based on the case where lateral flow rapid tests (LFTs) are provided to all individuals in the susceptible population and these people are freely able to self-test if they suspect they are symptomatic. We parameterise this as an exponential distribution, with rate (λ) 0.5, where most individuals will self-test very shortly after they become symptomatic (approximately 40% of cases will self-test within the first day of sympmtom onset), with a few people waiting a 2 or more days before testing (approximately 3% take longer than one week to take a self-test). We assume that LFTs are 100% accurate so all symptomatic individuals will receive a positive test result.

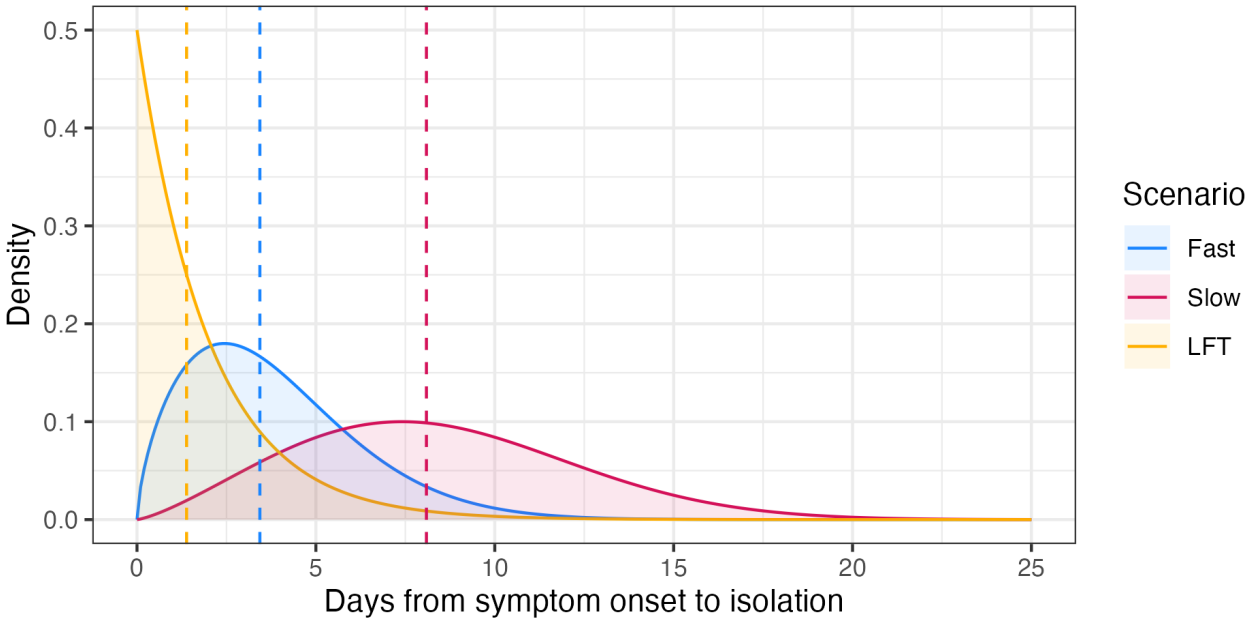

Figure 4: Three assumed onset-to-isolation delays used in the simuluation experiment. The *Fast* scenario is based on the onset-to-isolation for SARS-CoV-1 response in Hong Kong (Donnelly et al. 2003), the median onset-to-isolation time is 3.4 days (blue dashed line). The *Slow* scenario is based on the onset-to-isolation for the SARS-CoV-2 response in Wuhan, China (Li et al., 2020), the median onset-to-isolatiojn is 8.1 days (red dashed line). The lateral flow test (LFT) scenario is an assumed distributed for rapid self-administered home testing upon isolation, the median delay from symptom onset to isolation in this scenario is 1.4 days.

We define the proportion of pre-symptomatic transmission (θ) follwowing the approach of Hellewell et al. (2020) by parameterising a skew-normal distribution to sample the infection times using the incubation period and a shape parameter (α). The shape parameter controls the proportion of pre-symptomatic transmission by modulating the proportion of transmission times that are less than the incubation time (Figure 5). We parameterise the skew-normal with three proportion of presymptomatic transmission scenarios: <1%, 15%, 30%, these correspond to α values of 30, 1.95 and 0.7, respectively (Figure 5). Therefore, in all scenarios most transmission occurs after symptom onset, but due to isolation only impacting symptomatic individuals the greater proportion of transmission that occurs before symptom onset, the less effective contact tracing is hypothesied to be.

The proportion of pandemic-potential influenza infections that are asymptomatic varies for past outbreaks. There is evidence from past human outbreaks of H1N1pdm and H5N1 (2.3.4.4b) that some laboratory (polymerase chain reaction) positive cases showed no symptoms or symptoms too mild to be considered influenza-like illness (Lessler et al., 2009; Garg et al., 2025); but whether human-to-human transmission can occur while subclinical is unknown. There is no evidence of asymptomatic transmission for the H7N9 subtype (Xu et al., 2013). Here we assume that asymptomatic cases occur and can infect others, but are uncommon and that the majority of cases will develop symptoms during their infectious period. We ran three scenarios, one with zero asymptomatic tranmission, another with 10% of cases being asymptomatic and the most extreme scenario where 30% of cases never develop symptoms and thus are not isolated and secondary cases are missed by contact tracing.

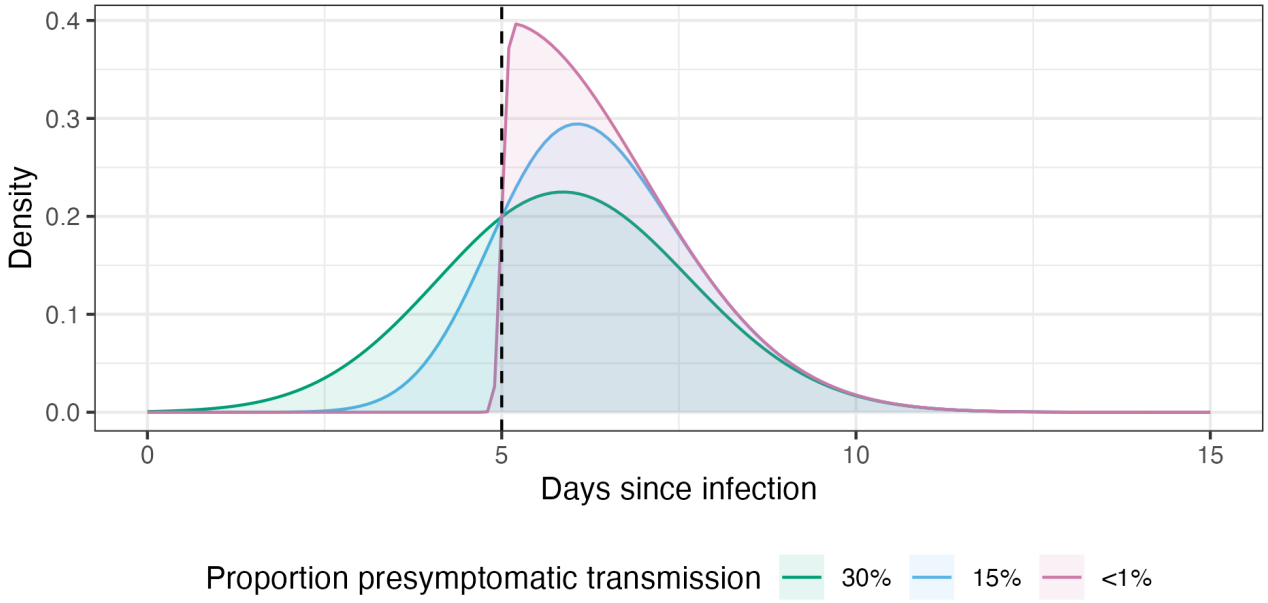

Figure 5: Proportion of presymptomatic transmission determined by the incubation period, here assumed to be 5 days (dashed vertical line), controlled by a skew-normal distribution.

We simulated scenarios with either 5, 20 or 40 initial cases. This is to test whether contact tracing can contain outbreaks that may have already accumulated cases before contact tracing is started, or represents importation of multiple cases in a single event, such as a flight with multiple infectors (Khanh et al. 2020).

The proportion of ascertainment is varied between 0 and 1, at intervals of 0.2, to test at what proportion of missed cases would lead to outbreaks becoming uncontrolled epidemics.

Some parameters we fixed across all simulations. The dispersion parameter for the negative binomial offspring distribution was fixed at 1 for isolated cases, 0.16 for subclinical and community cases. For computational efficiency we capped the maximum number of days the simulation could run for to 365. This is substantially longer than the 12-16 week window for evaluating outbreak control so does not influence the results. Additionally, we limit simulations to 500 cases. This is an arbitrary threshold we judge to be large epidemic that is not controllable.

Results

The incubation period for H1N1 is noticably shorter than the other two subtypes (H5N1 and H7N9), which are similar, with H5N1 having a slightly longer median (Figure 3).

Predictably, the ability to control an influenza epidemic is highly dependent on the reproduction number and the speed of isolation after symptom onset (Figure 6). A higher outbreak reproduction number results in a smaller percentage of outbreaks controlled at a given percentage of contacts traced, except in cases where they are equal because zero or all outbreaks are contained, across all onset-to-isolation scenarios (Figure 6). When the reponse to isolate cases is slow then outbreaks with $R = 1.5$ require at least 50% of contacts traced to contain at least half of simulated outbreaks. When R is 2.5 or 3.5 then contact tracing needs to be extremely comprehensive ($> 90\%$ to have a chance at containment, and even then $R = 3.5$ influenza outbreaks on average are uncontrolled (Figure 6A). Especially for H1N1, given it's faster tempo of transmission, having a much lower probability of containment at 100% of contacts traced with a slow, COVID-19-like, isolation response time (Figure 6A). In a scenario with a fast, Hong Kong SARS-like, onset-to-isolation response, outbreaks with $R = 1.1$ are almost always contained at any proportion of contacts traced (Figure 6B). For slow and fast isolation response delays there is a substantial difference between outbreaks with a R slightly above unity ($R = 1.1$) which were controlled at a low levels ($\geq 20\%$) of isolation and contact tracing for all three influenza subtypes (Figure 6A,B). As R increases to 1.5 there is a dramatic decline in the ability to control the epidemic without isolation of traced contacts (i.e. 0% control effectiveness), however, outbreaks with $R = 1.5$ are mostly contained once percentage of contacts ascertained in tracing exceeds 50% (Figure 6B). For more transmissible influenza scenarios, even a fast isolation response with an average of 3.4 days between symptom onset and isolation requires $> 70\%$ of contacts traced for most outbreaks to be controlled (Figure 6B).

The most rapid scenario we simulated to emulate individuals self-testing with LFTs, has the same trend of increased chance of outbreak containment by reducing the time between symptom onset and isolation, as the slow and fast scenarios (Figure 6). The contol of low transmissible ($R \in 1.1, 1.5$) influenza pathogens is almost always guranteed even in the absence of contact tracing and only isolating cases immediately if positive on an LFT (Figure 6C). Assuming ubiquitous access to home testing and that 63% of symptomatic cases testing and isolating within the 24 hours symptom onset, 75% ascertainment of contacts results in most outbreaks controlled for all influenza transmissibility scenarios ($R \leq 3.5$). The LFT isolation strategy is also the only onset-to-isolation delay which can achieve 100% of outbreaks controlled when all contacts are traced (Figure 6C).

The difference in influenza subtype incubation period influences the efficacy of isolating and tracing. This effect is most pronounced when the percentage of outbreaks controlled is greater than 0% and less than 100% (i.e. not at the boundary) (Figure 6). The shortest incubation period, H1N1, predominantly the least controllable for a given reproduction number, showing that infections that are symptomatic shortly after infection and in some instances transmission while subclinical limit our ability to effectively tracing and isolate their potential infectees in time to prevent disease transmission. The variance between the influenza subtypes at each percentage of contacts traced and isolated varies (i.e. difference between circle, triangle and square points at each contacts traced % in Figure 6). This variance is greatest at intermediate (20% - 80%) contact tracing effectiveness and intermediate values of R (1.5 and 2.5) (Figure 6). This could indicate a substantive role for incubation period durartion in the control of disease transmission. However, this variance in proportion of outbreaks controlled between pathogen subtypes does not show a strong pattern across all scenarios simulated (Figure S1). There is a weak pattern of increased variance in controllability between subtypes at intermediate values of R, overall it seems that incubation period causes differences in control-by-isolation effectivness when not at the boundary of epidemic controllability. In other words, differences between influenza subtypes arise when not in a situation of high transmissibility and low contact tracing effectivness that cannot contain any outbreaks, nor low transmissibility and high contact tracing effectivenss easily contain all outbreaks (Figure S1).

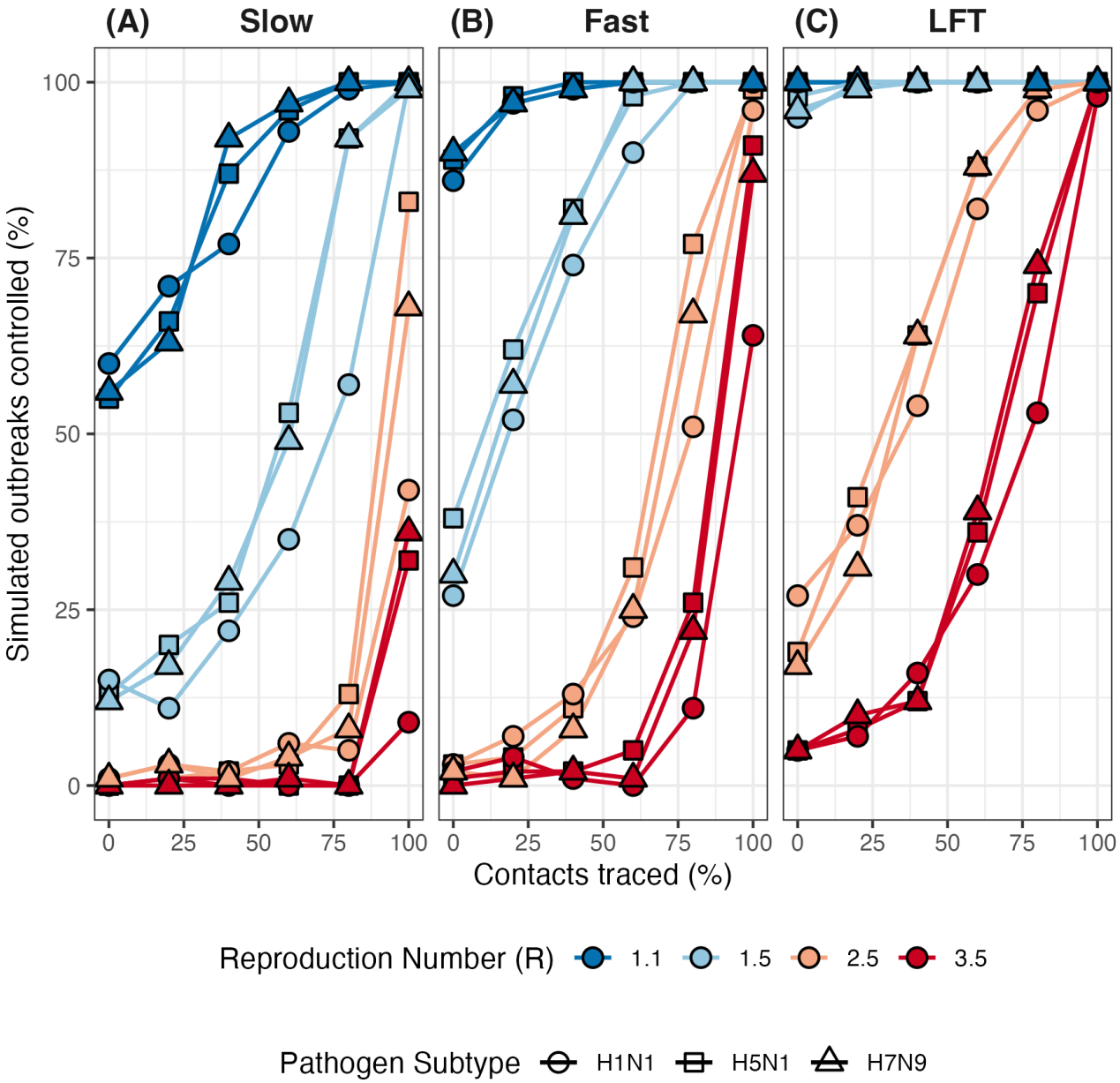

Figure 6: The percentage of outbreaks controlled across values of isolation and contact tracing effectiveness, for outbreaks with an assumed reproduction number (R) of either 1.1 or 1.5. This is for a baselines scenario where the number of initial cases is 10, the proportion of presymptomatic transmission is 15%, all cases are assumed symptomatic, and the onset-to-isolation delay is assumed to be SARS-like.

The pattern of outbreak control is broadly similar between 10% asymptomatic cases and the 0% and 30% asymptomatic scenarios (Figure S2). Qualitative difference are in the 30% asymptomatic scenario for LFT isolation, where the ability to control highly transmissible influenzas reduces to less than a quarter of outbreaks controlled at maxmimum contact tracing coverage (Figure S2). When every case is symptomatic the likelihood of containing highly transmissible outbreaks drastically increases for all onset-to-isolation response delays (Figure S2).

The proportion of transmission that occurs before on the onset of symptoms has a moderate affect on epidemic containment for across isolation response rates (Figure S3). In all scenarios decreasing the proportion of presympatomatic transmission result in an greater or equal probability of outbreak control. When presymptomatic transmission is minimal, most $R = 1.1$ outbreaks go extinct without any contact tracing, at any rate of isolation after symptom onset, with extinction ensured if isolated after LFT testing (Figure S3 leftmost column). Furthermore, when $< 1\%$ of transmission is presymptomatic, rapidly isolating after symptoms (e.g. after self-testing) can contain more than half of outbreaks for all transmissibility scenarios ($R \leq 3.5$) (Figure S3). Conversely, when 30% of transmission is presymptomatic, less than half of highly transmissible epidemics are controlled, even with the most optimistic isolation response time and contact tracing coverage (Figure S3 rightmost column).

The ability to control an epidemic that can readily transmit human-to-human is moderated by the initial number of infectious individuals that seed the outbreak. The higher the number of cases the less chance that stochastic extinction of a transmission chain will end the whole epidemic. For an influenza pandemic, the number of initial infected individuals influences efficacy of control-by-isolation at all transmissibility scenarios evaluated ($R \in \{1.1, 1.5, 2.5, 3.5\}$, Figure 7). When $R = 1.1$ most outbreaks can be controlled without isolation and contact tracing, even with 40 initial infectors Figure 7). When $R = 1.5$ the increase in the number of initial infections from 5 to 20 has a large decrease in outbreaks controlled at low levels of contact tracing, the same pattern when the number of initial infectors is twofold larger at 40, but these differences in outbreak control diminish as contact tracing increases towards 100% (Figure 7). When the number of cases seeding the outbreak is > 20 at $R > 2.5$ a large proportion of outbreaks become uncontrollable until contact tracing reaches $> 60\%$. In the worst case transmissibility scenario ($R = 3.5$) if contact tracing is not activated until at least 20 individuals are infected then close to 100% of contacts with need to be traced in order to control the majority of outbreaks (Figure 7).

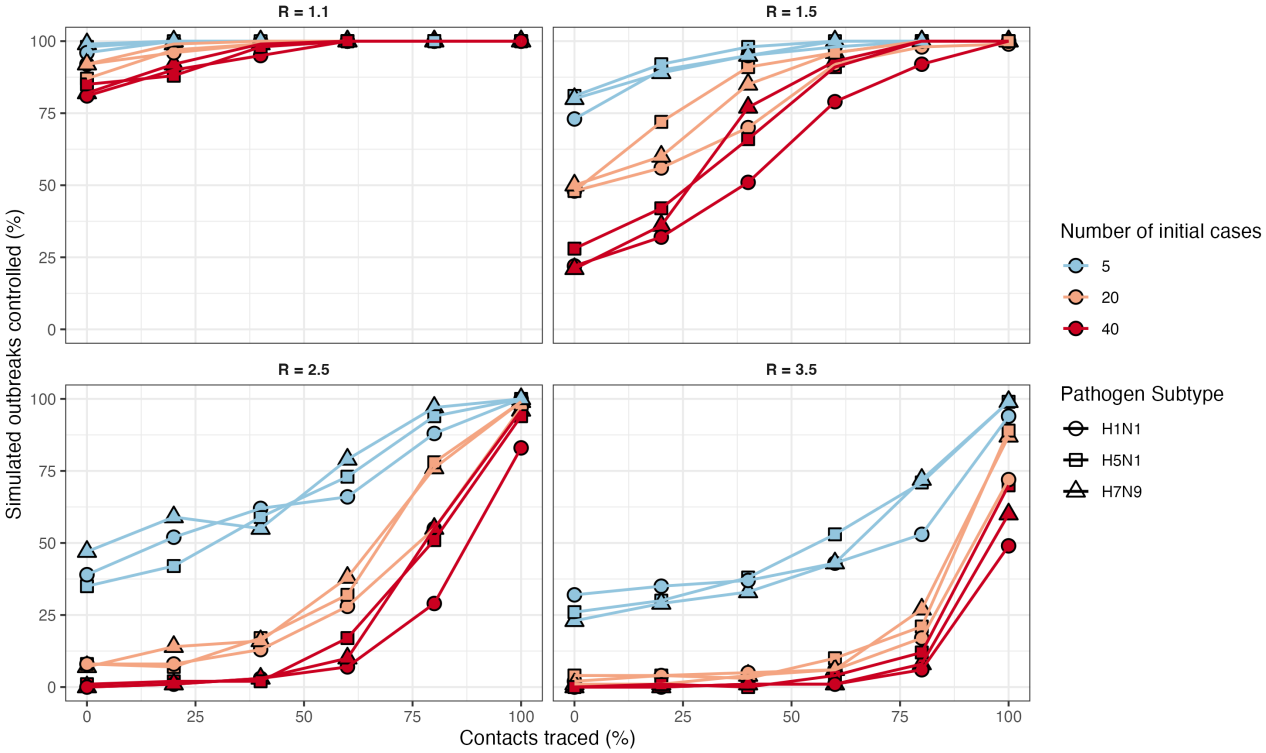

Figure 7: The percentage of outbreaks controlled across values of isolation and contact tracing effectiveness, for outbreaks with an initial number of seeding infections assumed to be either 5 or 10. This is for a baselines scenario where the reproduction number is 1.5, the proportion of presymptomatic transmission is 15%, all cases are assumed symptomatic, and the onset-to-isolation delay is assumed to be SARS-like.

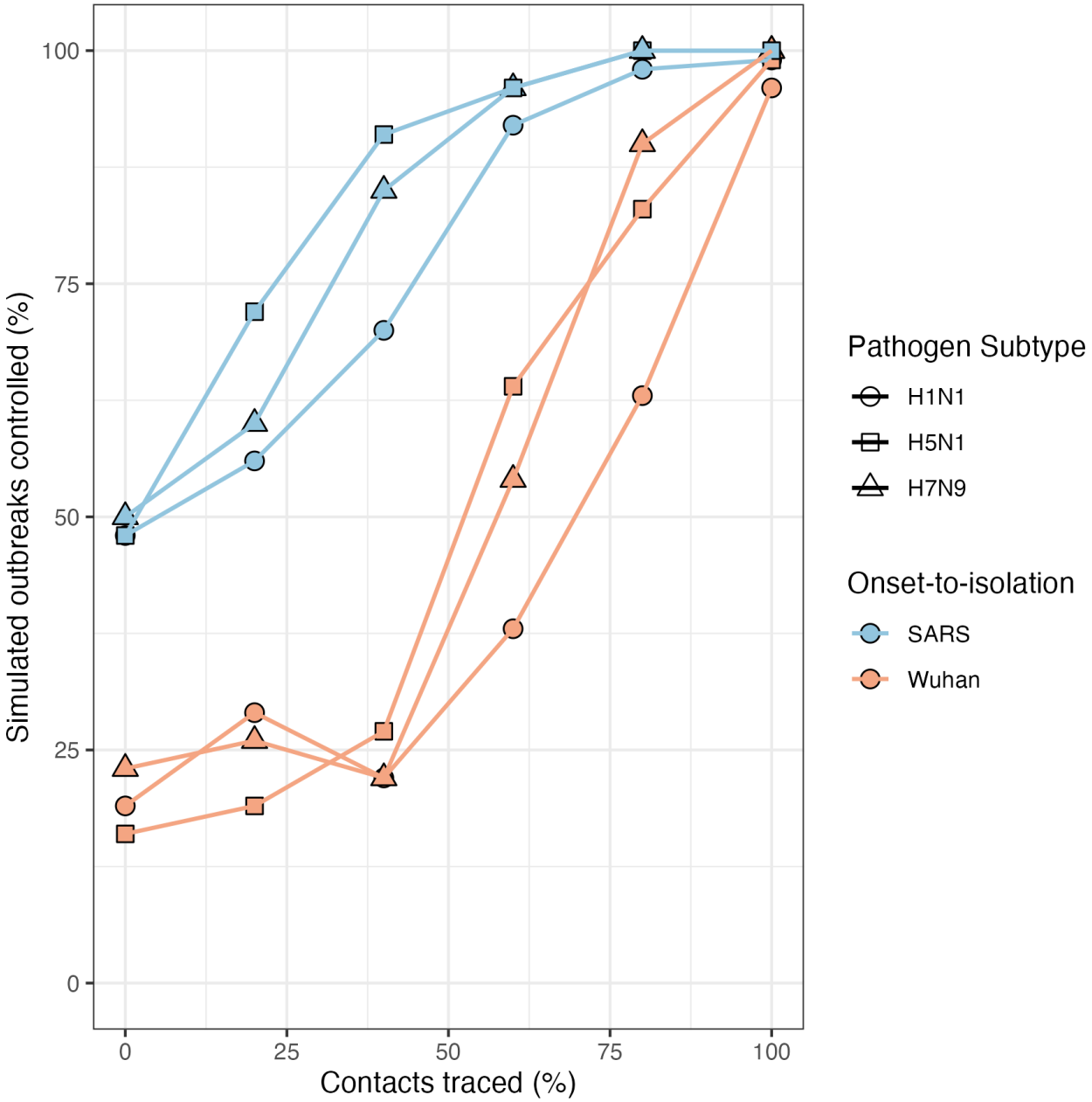

Figure 8: The percentage of outbreaks controlled across values of isolation and contact tracing effectiveness, for outbreaks with an onset-to-isolation delay distribution that is either SARS-like, or COVID-19-like (from Wuhan). This is for a baselines scenario where the reproduction number is 1.5, the proportion of presymptomatic transmission is 15%, all cases are assumed symptomatic, and the number of initial infections is 10.

Discussion

- This study has looked at the feasibility and effectiveness of isolation and contact tracing for influenza subtypes that have cause epidemic outbreaks.
- Outbreaks controlled at 50% of contacts traced and isolated is over ??%, highlighting the effectiveness of this intervention for infectious diseases are not highly transmissible between humans.
- Discuss the existing flu vaccines and antivirals that can be used an interventions in addition to NPIs
- In modelling the effectiveness of isolation and contact tracing we have assumed that there is no capacity limits on contact tracing, which does not hold in large outbreaks such as SARS-CoV-2 (ref). We also ignore potential socio-political factors that would prevent health worker from visiting or contacting infected individuals or contacts of

infected individuals (Dhillon and Kelly, 2018). We also did not consider zoonotic spillover infections or formite transmission.

- Digital tracing has capacity for large-scale contact tracing (pingdemic), also rapid tests are a complementary approach for limiting spread.
- In this study we model isolation and contact tracing as the sole intervention in containing an influenza outbreak. This is to provide an assessment of its effectiveness for rapidly transmission and potentially highly transmissible subtypes. However, in reality, pandemic preparedness to a pandemic potential influenza would not need to deploy interventions, such as contact tracing individually or sequentially, instead they can be used in combination, such as antivirals (e.g. oseltamivir), rapid tests, contact tracing, and vaccination.
- Antivirals for half the UK, these can be deployed in rapid response to flu pandemic.
- In this study we have parameterised the transmission model with parameter from avian influenza subtypes (H5N1 and H7N9) and a influenza subtype that caused an epidemic in the recent past (H1N1), and response delays from SARS and COVID-19 outbreaks. However, these results can be used to inform other influenza subtypes that exhibit similar epidemiological characteristics in transmissibility and severity from past outbreaks (H2N2 and H3N2) and still exist in animal reservoirs for potential spillovers back into human populations (ref).
- This study used a branching process model to simulate individual-level transmission and intervention. The model assumes an infinite population size with no interdependence of isolation and contact tracing between cases whereby a case may be in contact with multiple infectors and only needs to be traced in time by one contact to prevent transmission, as could happened in a fixed random network transmission model. It is unlikely that this model structure difference would have a considerable different on our results for the control of disease outbreaks with contact tracing. We suppose that because our model requires isolation sampled for a single individual, our results are more conservative on the ability to control outbreaks, and that using a random network model would indicate an increased effectivness of contact tracing (Juul and Strogatz, 2023). The infinite population assumption also means that although isolated individuals are assumed to not transmit, there are always other individuals that non-isolated infectors can transmit to, whereas a fixed random network model that assumes optimal indefinite isolation will block of parts of the network and overestimate contact tracing effectiveness (Juul and Strogatz, 2023).
- The reproduction number for H5N1 (including clade 2.3.4.4b) and H7N9 influenza subtypes have been estimated to be far below 1 (Ward et al., Garg et al., 2025). Therefore, the transmissibility scenarios explored in this study are speculative and assume that pathogen evolution increases human-to-human transmission potential. If transmissibility of these avian influenza subtypes remains constant over time then outbreaks are expected to be subcritical and will not produce epidemics and thus not require interventions. If cases of avian influenza are detected with routine surveillance without a known animal source, it may indicate sustained human-to-human transmission and can be a trigger to commence isolation and contact tracing while the number of initial cases is presumed small, which as we show increases epidemic controllability (Figure 7).
- This study has evaluated the ability to control the outbreak of an infectious disease independent on its severity. Infection severity and fatality risks are of course critical when formulating a pandemic response plan. By understanding the efficacy of isolation and contact trace for a given epidemiological characterstic, outbreak mortality and morbidity can hopefully be minimised by reducing disease incidence over time to elimination.
- Our branching process model used a simple forward contact-tracing mechanism that reduces the number of secondary contacts based on the timing of isolation of symptomatic cases. This contact tracing stragety is minimal cost and effort. In scenarios where outbreaks are uncontrolled a more comprehensive and costly contact tracing system where infectors and contacts of infectors (i.e. backward and forward contact tracing) are followed up, which has been shown to be more effective at outbreak containment (Klinkenberg et al., 2006).
- Isolation and contact tracing complementing in combination with other quickly available measures for pandemic potential influenza strains, such as rapid testing and antivirals (Hayden, 2001).

References

Tjandra Y. Aditama, Gina Samaan, Rita Kusriastuti, Ondri Dwi Sampurno, Wilfried Purba, null Misriyah, Hari Santoso, Arie Bratasena, Anas Maruf, Elvieda Sariwati, Vivi Setiawaty, Kathryn Glass, Kamalini Lokuge, Paul M. Kelly, and I. Nyoman Kandun. Avian influenza H5N1 transmission in households, Indonesia. *PloS One*, 7(1):e29971, 2012. ISSN 1932-6203. doi: 10.1371/journal.pone.0029971.

A. Azzalini. A Class of Distributions Which Includes the Normal Ones. *Scandinavian Journal of Statistics*, 12(2):171–178, 1985.

David M. Bell and World Health Organization Working Group on International and Community Transmission of SARS. Public health interventions and SARS spread, 2003. *Emerging Infectious Diseases*, 10(11):1900–1906, November 2004. ISSN 1080-6040. doi: 10.3201/eid1011.040729.

Benjamin J. Cowling, Lianmei Jin, Eric H. Y. Lau, Qiaohong Liao, Peng Wu, Hui Jiang, Tim K. Tsang, Jiandong Zheng, Vicky J. Fang, Zhaorui Chang, Michael Y. Ni, Qian Zhang, Dennis K. M. Ip, Jianxing Yu, Yu Li, Liping Wang, Wenxiao Tu, Ling Meng, Joseph T. Wu, Huiming Luo, Qun Li, Yuelong Shu, Zhongjie Li, Zijian Feng, Weizhong Yang, Yu Wang, Gabriel M. Leung, and Hongjie Yu. Comparative epidemiology of human infections with avian influenza A H7N9 and H5N1 viruses in China: A population-based study of laboratory-confirmed cases. *Lancet (London, England)*, 382(9887): 129–137, July 2013. ISSN 1474-547X. doi: 10.1016/S0140-6736(13)61171-X.

Ranu S Dhillon and Devabhaktuni Srikrishna. When is contact tracing not enough to stop an outbreak? *The Lancet Infectious Diseases*, 18(12):1302–1304, December 2018. ISSN 14733099. doi: 10.1016/S1473-3099(18)30656-X.

C. P. Farrington and A. D. Grant. The distribution of time to extinction in subcritical branching processes: Applications to outbreaks of infectious disease. *Journal of Applied Probability*, 36(3):771–779, September 1999. ISSN 0021-9002, 1475-6072. doi: 10.1239/jap/1032374633.

Neil M. Ferguson, Derek A. T. Cummings, Christophe Fraser, James C. Cajka, Philip C. Cooley, and Donald S. Burke. Strategies for mitigating an influenza pandemic. *Nature*, 442(7101):448–452, July 2006. ISSN 1476-4687. doi: 10.1038/nature04795.

Luca Ferretti, Chris Wymant, Michelle Kendall, Lele Zhao, Anel Nurtay, Lucie Abeler-Dörner, Michael Parker, David Bonsall, and Christophe Fraser. Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing. *Science*, 368(6491), May 2020. ISSN 0036-8075, 1095-9203. doi: 10.1126/science.abb6936.

William H. Foege, J. Donald Millar, and J. Michael Lane. SELECTIVE EPIDEMIOLOGIC CONTROL IN SMALLPOX ERADICATION1. *American Journal of Epidemiology*, 94(4):311–315, October 1971. ISSN 1476-6256, 0002-9262. doi: 10.1093/oxfordjournals.aje.a121325.

Christophe Fraser, Steven Riley, Roy M. Anderson, and Neil M. Ferguson. Factors that make an infectious disease outbreak controllable. *Proceedings of the National Academy of Sciences of the United States of America*, 101(16):6146–6151, April 2004. ISSN 0027-8424. doi: 10.1073/pnas.0307506101.

Christophe Fraser, Christl A. Donnelly, Simon Cauchemez, William P. Hanage, Maria D. Van Kerkhove, T. Déirdre Hollingsworth, Jamie Griffin, Rebecca F. Baggaley, Helen E. Jenkins, Emily J. Lyons, Thibaut Jombart, Wes R. Hinsley, Nicholas C. Grassly, Francois Balloux, Azra C. Ghani, Neil M. Ferguson, Andrew Rambaut, Oliver G. Pybus, Hugo Lopez-Gatell, Celia M. Alpuche-Aranda, Ietza Bojorquez Chapela, Ethel Palacios Zavala, Dulce Ma Espejo Guevara, Francesco Checchi, Erika Garcia, Stephane Hugonnet, Cathy Roth, and WHO Rapid Pandemic Assessment Collaboration. Pandemic potential of a strain of influenza A (H1N1): Early findings. *Science (New York, N.Y.)*, 324(5934):1557–1561, June 2009. ISSN 1095-9203. doi: 10.1126/science.1176062.

Shikha Garg, Katie Reinhart, Alexia Couture, Krista Kniss, C. Todd Davis, Marie K. Kirby, Erin L. Murray, Sophie Zhu, Vit Kraushaar, Debra A. Wadford, Cara Drehoff, Allison Kohnen, Mackenzie Owen, Jennifer Morse, Seth Eckel, Jessica Goswitz, George Turabelidze, Steve Krager, Anna Unutzer, Emilio R. Gonzales, Cherissa Abdul Hamid, Sascha Ellington, Alexandra M. Mellis, Alicia Budd, John R. Barnes, Matthew Biggerstaff, Michael A. Jhung, Malia Richmond-Crum, Erin Burns, Tom T. Shimabukuro, Timothy M. Uyeki, Vivien G. Dugan, Carrie Reed, and Sonja J. Olsen. Highly Pathogenic Avian Influenza A(H5N1) Virus Infections in Humans. *New England Journal of Medicine*, 392(9):843–854, February 2025. ISSN 0028-4793, 1533-4406. doi: 10.1056/NEJMoa2414610.

F. G. Hayden. Perspectives on antiviral use during pandemic influenza. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, 356(1416):1877–1884, December 2001. ISSN 0962-8436. doi: 10.1098/rstb.2001.1007.

Joel Hellewell, Sam Abbott, Amy Gimma, Nikos I Bosse, Christopher I Jarvis, Timothy W Russell, James D Munday, Adam J Kucharski, W John Edmunds, Sebastian Funk, Rosalind M Eggo, Fiona Sun, Stefan Flasche, Billy J Quilty, Nicholas Davies, Yang Liu, Samuel Clifford, Petra Klepac, Mark Jit, Charlie Diamond, Hamish Gibbs, and Kevin Van Zandvoort. Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. *The Lancet Global Health*, 8(4):e488–e496, April 2020. ISSN 2214109X. doi: 10.1016/S2214-109X(20)30074-7.

Joel Hellewell, Sam Abbott, Amy Gimma, Tim Lucas, Sebastian Funk, and Adam Kucharski. *Ringbp: Simulate and Evaluate Contact Tracing Scenarios*, 2025.

Niall P. A. S. Johnson and Juergen Mueller. Updating the Accounts: Global Mortality of the 1918-1920 "Spanish" Influenza Pandemic. *Bulletin of the History of Medicine*, 76(1):105–115, March 2002. ISSN 1086-3176. doi: 10.1353/bhm.2002.0022.

Matt J Keeling, T Deirdre Hollingsworth, and Jonathan M Read. Efficacy of contact tracing for the containment of the 2019 novel coronavirus (COVID-19). *Journal of Epidemiology and Community Health*, 74(10):861–866, October 2020. ISSN 0143-005X, 1470-2738. doi: 10.1136/jech-2020-214051.

Don Klinkenberg, Christophe Fraser, and Hans Heesterbeek. The Effectiveness of Contact Tracing in Emerging Epidemics. *PLoS ONE*, 1(1):e12, December 2006. ISSN 1932-6203. doi: 10.1371/journal.pone.0000012.

Adam J. Kucharski. Controlling minor outbreaks is necessary to prepare for major pandemics. *PLOS Biology*, 22(12): e3002945, December 2024. ISSN 1545-7885. doi: 10.1371/journal.pbio.3002945.

Adam J. Kucharski, Rosalind M. Eggo, Conall H. Watson, Anton Camacho, Sebastian Funk, and W. John Edmunds. Effectiveness of Ring Vaccination as Control Strategy for Ebola Virus Disease. *Emerging Infectious Diseases*, 22(1):105–108, January 2016. ISSN 1080-6040, 1080-6059. doi: 10.3201/eid2201.151410.

Adam J Kucharski, Timothy W Russell, Charlie Diamond, Yang Liu, John Edmunds, Sebastian Funk, Rosalind M Eggo, Fiona Sun, Mark Jit, James D Munday, Nicholas Davies, Amy Gimma, Kevin Van Zandvoort, Hamish Gibbs, Joel Hellewell, Christopher I Jarvis, Sam Clifford, Billy J Quilty, Nikos I Bosse, Sam Abbott, Petra Klepac, and Stefan Flasche. Early dynamics of transmission and control of COVID-19: A mathematical modelling study. *The Lancet Infectious Diseases*, 20 (5):553–558, May 2020. ISSN 14733099. doi: 10.1016/S1473-3099(20)30144-4.

Justin Lessler, Nicholas G. Reich, Derek A. T. Cummings, New York City Department of Health and Mental Hygiene Swine Influenza Investigation Team, H. P. Nair, H. T. Jordan, and N. Thompson. Outbreak of 2009 pandemic influenza A (H1N1) at a New York City school. *The New England Journal of Medicine*, 361(27):2628–2636, December 2009. ISSN 1533-4406. doi: 10.1056/NEJMoa0906089.

J. O. Lloyd-Smith, S. J. Schreiber, P. E. Kopp, and W. M. Getz. Superspreading and the effect of individual variation on disease emergence. *Nature*, 438(7066):355–359, November 2005. ISSN 0028-0836, 1476-4687. doi: 10.1038/nature04153.

Hiroshi Nishiura and Hisashi Inaba. Estimation of the incubation period of influenza A (H1N1-2009) among imported cases: Addressing censoring using outbreak data at the origin of importation. *Journal of Theoretical Biology*, 272(1):123–130, March 2011. ISSN 1095-8541. doi: 10.1016/j.jtbi.2010.12.017.

Adriana Reyna-Lara, David Soriano-Paños, Sergio Gómez, Clara Granell, Joan T. Matamalas, Benjamin Steinegger, Alex Arenas, and Jesús Gómez-Gardeñes. Virus spread versus contact tracing: Two competing contagion processes. *Physical Review Research*, 3(1):013163, February 2021. ISSN 2643-1564. doi: 10.1103/PhysRevResearch.3.013163.

W. D. Tanner, D. J. A. Toth, and A. V. Gundlapalli. The pandemic potential of avian influenza A(H7N9) virus: A review. *Epidemiology and Infection*, 143(16):3359–3374, December 2015. ISSN 1469-4409. doi: 10.1017/S0950268815001570.

Jack Ward, Joshua W. Lambert, Timothy W. Russell, James M. Azam, Adam J. Kucharski, Sebastian Funk, Billy J. Quilty, Oswaldo Gressani, Niel Hens, and W. John Edmunds. Estimates of epidemiological parameters for H5N1 influenza in humans: A rapid review. *medRxiv : the preprint server for health sciences*, 2024. doi: 10.1101/2024.12.11.24318702.

Charles Whittaker, Gregory Barnsley, Daniela Olivera Mesa, Daniel J Laydon, Chee Wah Tan, Feng Zhu, Rob Johnson, Patrick Doohan, Gemma Nedjati-Gilani, Peter Winskill, Alexandra B. Hogan, Arminder Deol, Christinah Mukandavire, Katharina Hauck, David Chien Boon Lye, Lin-Fa Wang, Oliver J. Watson, and Azra C Ghani. Quantifying the impact of a broadly protective sarbecovirus vaccine in a future SARS-X pandemic, August 2024.

WHO COVID-19 Dashboard. COVID-19 deaths | WHO COVID-19 dashboard. https://data.who.int/dashboards/covid19/cases.

WHO Ebola Response Team. Ebola Virus Disease in West Africa — The First 9 Months of the Epidemic and Forward Projections. *New England Journal of Medicine*, 371(16):1481–1495, October 2014. ISSN 0028-4793, 1533-4406. doi: 10.1056/nejmoa1411100.

W. Xu, L. Lu, B. Shen, J. Li, J. Xu, and S. Jiang. Serological Investigation of Subclinical Influenza A(H7H9) Infection Among Healthcare and Non-Healthcare Workers in Zhejiang Province, China. *Clinical Infectious Diseases*, 57(6):919–921, September 2013. ISSN 1058-4838, 1537-6591. doi: 10.1093/cid/cit396.

Yang Yang, M. Elizabeth Halloran, Jonathan D. Sugimoto, and Ira M. Longini. Detecting human-to-human transmission of avian influenza A (H5N1). *Emerging Infectious Diseases*, 13(9):1348–1353, September 2007. ISSN 1080-6040. doi: 10.3201/eid1309.070111.

Supplementary Material

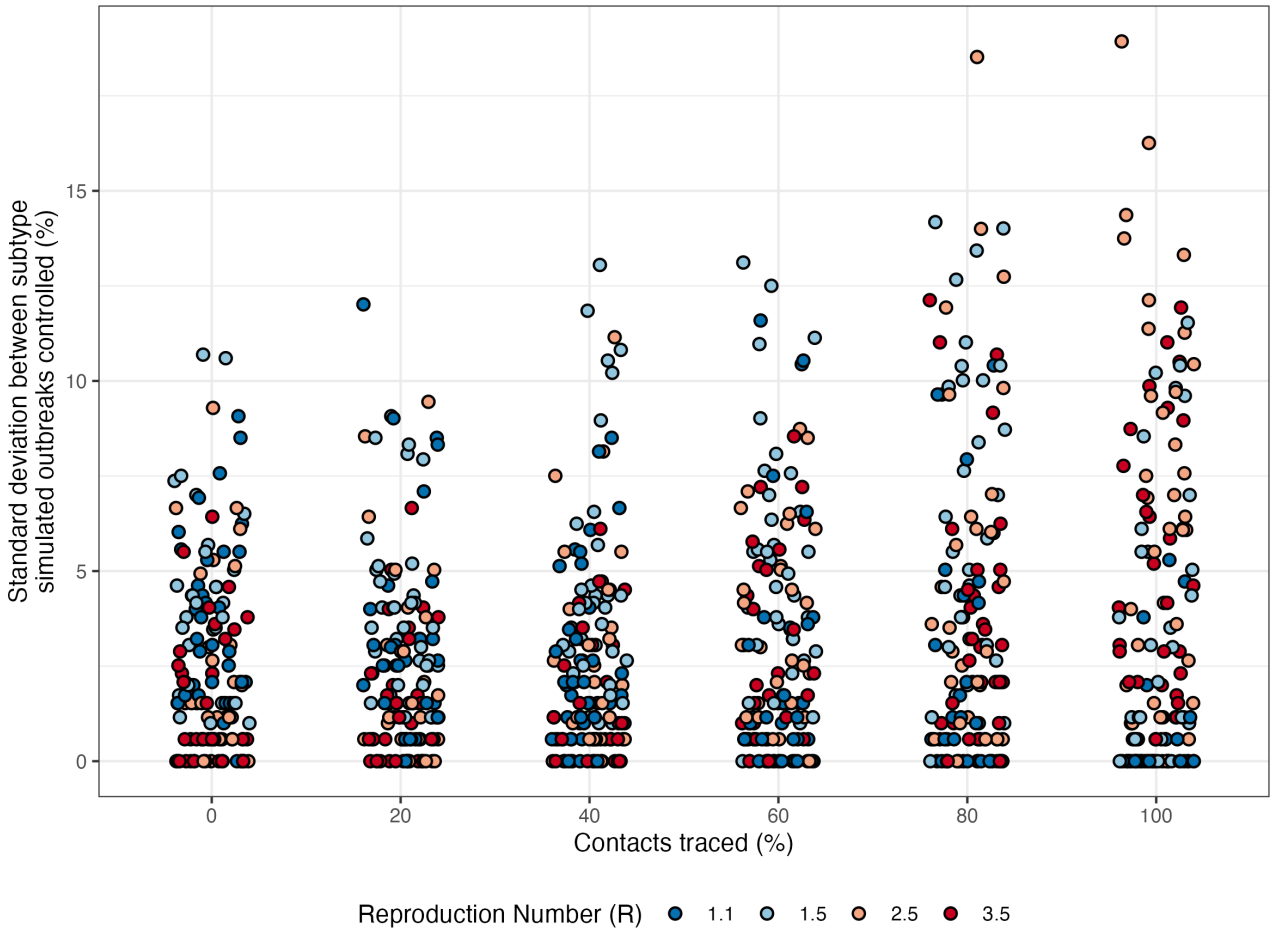

Figure S1: The standard deviation of the percentage of outbreaks controlled between influenza subtypes (H1N1, H5N1, H7N9), across percentages of contacts traced. Points are jittered horizontally reduce overlap.

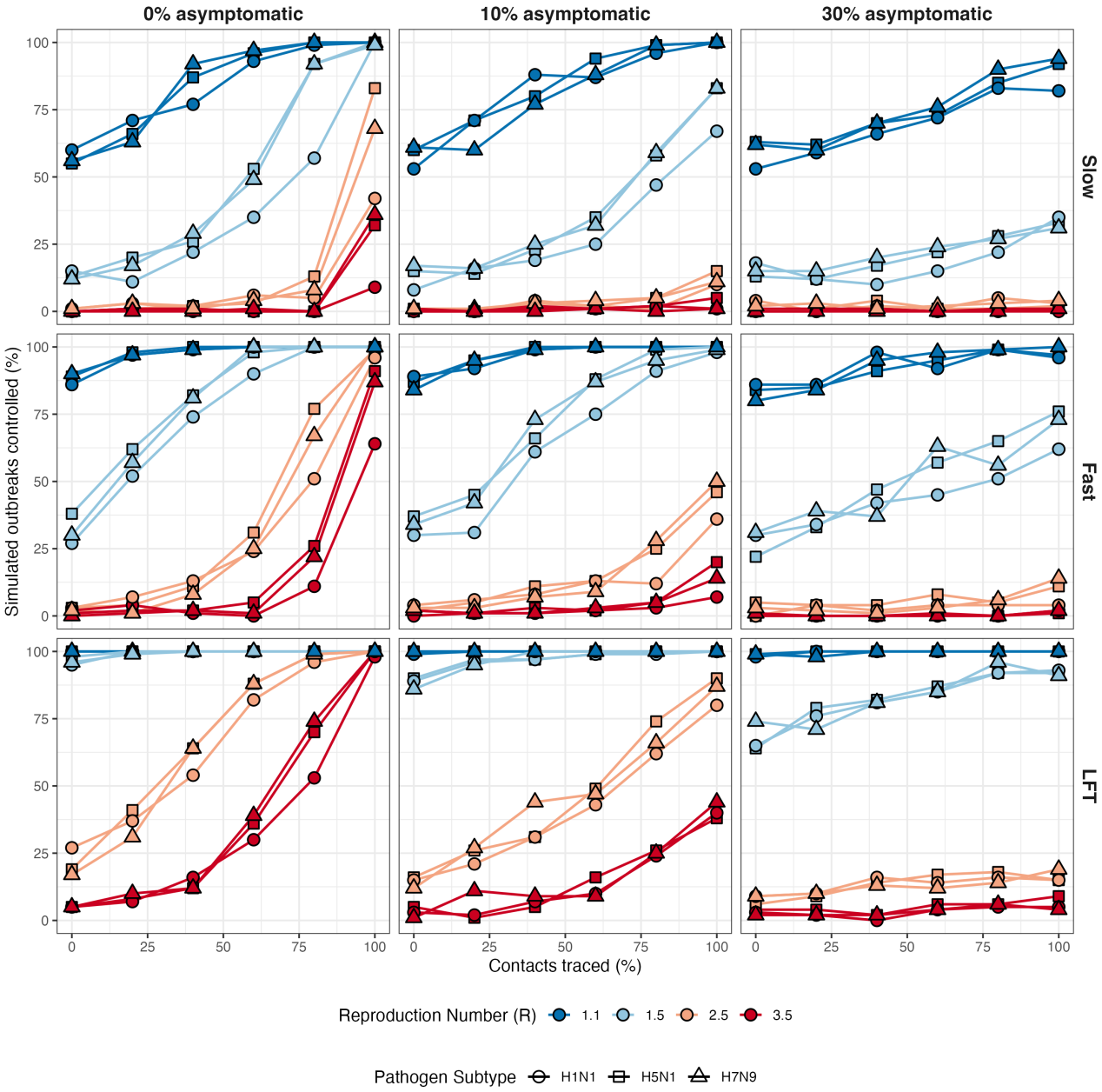

Figure S2: Stub.

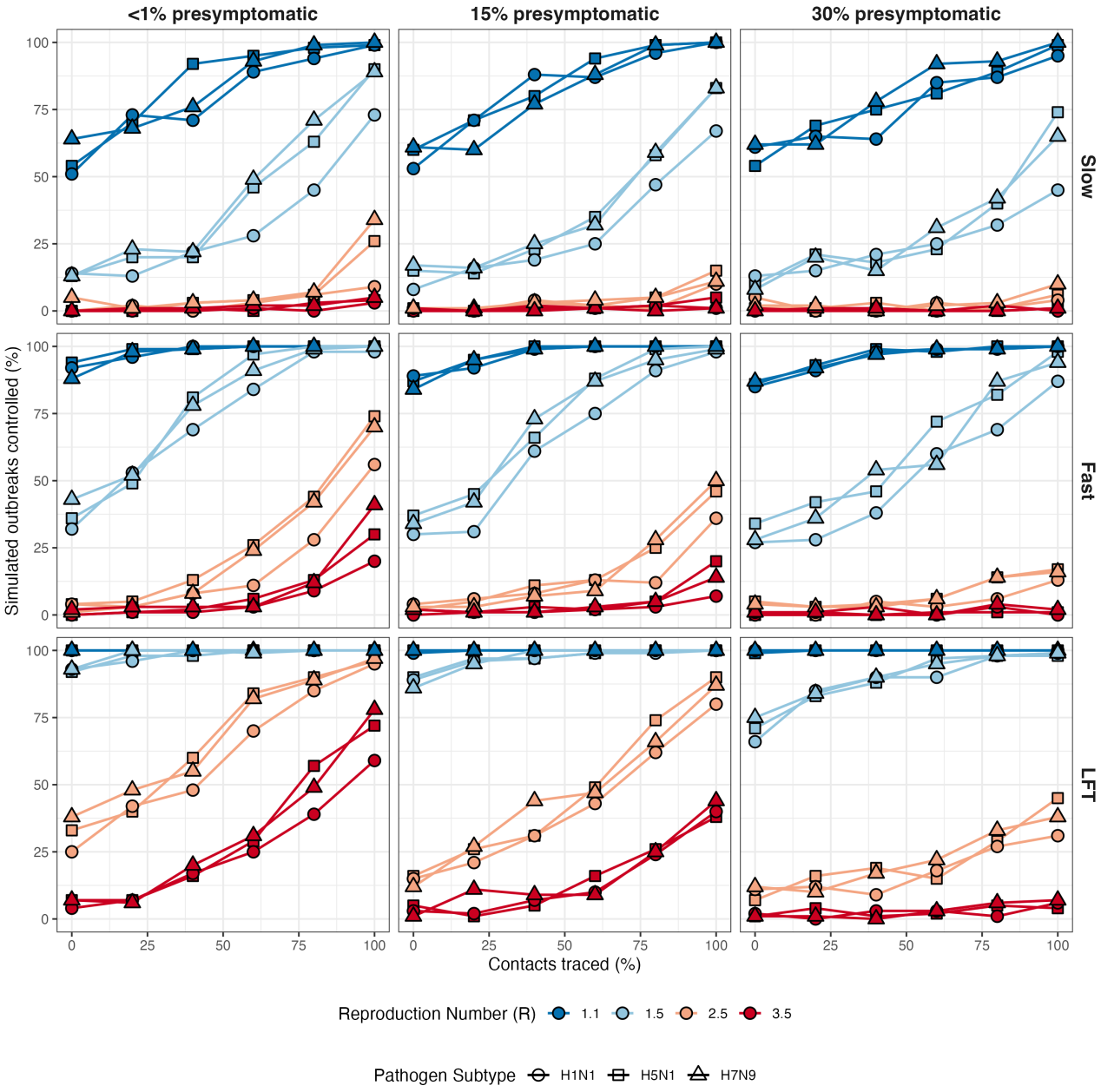

Figure S3: Stub.